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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,763	02/26/2002	Pentti Sipponen	0933-0181P	3752

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,763	SIPPONEN ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *4 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/28/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I encompassing claims 1-3 in the reply filed on 10/04/2004 is acknowledged. The traversal is on the ground(s) that the invention is directed to a method for identifying an individual at risk for vascular and cancer disease, not a method of determining pepsinogen I and homocysteine levels or means for determining those levels. The invention as a whole does constitute a contribution over the prior art. This is not found persuasive because PCT Rule 13.2 and 37 C.F.R. 1.475 define "special technical feature " as those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." 37 C.F.R. 1.475(d) states that, if multiple products, processes of manufacture, or uses are claimed, the first mentioned in the claims will be considered as the main invention, along with each of the other categories related thereto. The main invention is method of determinng both serum pepsinogen and homocystein levels and the method had been described as stated in the ISR and reiterated in the previous Office action. Because the claimed technical feature does not define a contribution over the prior art, the main invention lacks a "special technical feature," unity of invention is lacking and restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 4, and 5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-5 are pending and examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "selecting a method specific cut-off for the said analyte" in lines 5-7, but it is not clear what the metes and bounds are. WO 96/15456 (23 May 1996, IDS) at pages 8-11 discloses different methods of determining pepsinogen A level in serum. Does the limitation mean a selecting a specific method for example ELISA vs. the first method at page 7 of WO 96/15456?

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the conclusion step linking the active step of the instant claim i.e. measuring vitamin B12 level to the purpose set out in the preamble of the base claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/15456 (23 May 1996, IDS) in view of Nexo et al., (IDS filed on 02/28/2002, Scand J Clin Lab Invest, vol. 54, Suppl. 219, pages 61-76).

Claims 1-3 are interpreted as drawn to method for identifying an individual at risk for cancer and vascular disease with the active step comprising detecting serum homocysteine and pepsinogen I levels in said individual, wherein detection of a high serum homocysteine level and a low serum pepsinogen I level, as compared to a reference value (normal range) is concluded as indicating said individual at risk for cancer and vascular disease, wherein vitamin B12 level is also measured in a individual (claim 3).

WO 96/15456 (IDS filed on 02/28/2002, 05/23/1996) at page 3 lines 1-12 teaches that gastric atrophy precedes gastric cancer, and an individual with low serum pepsinogen I is at risk of gastric cancer (see pages 7-11), and further teaches that the lower production of pepsinogen I, leads to vitamin B12 absorption disturbance, which in

turn leads to pernicious anemia. WO 96/15456 teaches two different methods of measuring pepsinogen I level.

WO 96/15456 does not teach the relationship between high serum homocystein level and risk for cancer and vascular diseases.

However, Nexo et al., (IDS filed on 02/28/2002, Scand J Clin Lab Invest, vol. 54, Suppl. 219, pages 61-76) teach homocysteine accumulation in patients with vitamin B12 (cobalamin) deficiency. In other word, Nexo et al., suggest that peptsinogen I not being produced normally in gastric atrophy preceding gastric cancer is the starting point that sets the downstream cascade, i.e., vitamin B12 deficiency associated pernicious anemia, and high accumulation of homocysteine. Nexo et al., teach measuring plasma homocystein level (note the paragraph bridging left and right columns of page 70 to 1st paragraph of right column of page 70), as well as the normal range of homocytein level for age, sex, other normal physiologic difference such as pregnancy has been determined and well known in the art before the effective filing date of the instant application. Nexo et al., at page 70 teach that increase in plasma homocystein ("P-HCY") is observed in patients with cobalamine deficiency, patients with coronary, cerebrovascular, or peripheral arterial disease, as well as patients with leukemia or solid tumors.

Nexo et al., teach measuring plasma pepsinogen A level (note page 72, right column, 3rd and 4th columns) had been known in the art before the effective filing date of the instant application.

Nexo et al., at page 72 right column, 3rd paragraph, also teach that "a low P (i.e. plasma)-Pepsinogen A in a clinical material of patients with suspected cobalamin deficiency is about 90% in severe gastric body atrophy, but only about 10% in patients with mild atrophy." It is noted that pepsinogen I and pepsinogen A are the same entity according to OMIM #1697000 downloaded from url>>www.ncbi.nlm.nih.gov on 12/16/04.

Nexo et al., from page 66 under the heading "Plasma cobalamins" to page 69 teach measuring plasma cobalmins (alias vitamin B12, see page 61, right column, the first line under the heading "Physiology of cobalamin uptake and utilization) is well known in the art.

Nexo et al., teach at page 64, right column, 4th paragraph that "[t]he anemia develops because the lack of cobalaim causes a retarded DNA synthesis with little effect on RNA and protein synthesis. The bone marrow becomes megaloblastic, due to an unbalanced cell growth and the result is macrocytic anemia, and often leukopenic and/or throbocytopenia." In summary, Nexo et al., teach that high plasma homocystein level is associated with cobalamin deficiency as well as cancer and vascular diseases, and low pepsinogen I level is associated with cobalamin deficiency.

Therefore, it would have obvious for one of ordinary skill to practice the claimed method with a reasonable expectation of success, given the method of testing both serum pepsinogen I and homocystein levels had been well known in the art before the effective filing date of the instant application. Given that low serum pepsinogen I level and high homocysteine level in serum are closely related to cancer and vascular

diseases as taught by Nexo et al., one of ordinary skill would be motivated to practice the instantly claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

MISOOK YU
PATENT EXAMINER